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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Jarrell *et al.*  
Serial No.: 09/478,263  
Filed: January 5, 2000  
For: COMBINATORIAL BIOLOGY

Examiner: Epperson, Jon D.  
Group Art Unit: 1639

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Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

**RESPONSE TO ELECTION OF SPECIES REQUIREMENT**

This Response to Election of Species Requirement is submitted in response to the Office Action mailed on January 6, 2003 for the above-identified application.

The Examiner has withdrawn all previous species elections and issued a substituted election of species. Telephone interviews between Examiner Epperson and Theresa A. Devlin, attorney for Applicants, were conducted on May 5, 2003 and May 6, 2003 to discuss how to proceed with an election of species when only generic terminology was used in the specification and claims. Examiner Epperson stated that where only generic terminology was used in the specification and claims Applicants could point out this out instead of electing a species.

Applicants traverse the election of species in regard to subgroups 1-5 and 7-13. As Applicants stated in the telephone interviews with the Examiner, Applicants believe that election of a species of enzymatic machinery (subgroup 6) would reduce the Examiner's search burden such that it would not be an undue burden. For example, when Applicants searched the USPTO patent application full text database for the term "peptide synthetase" from 1976 to the present, Applicants found that only 34 patents contained this term many of which had an effective filing date that was after Applicants' effective filing date (see Exhibit A). In addition, when Applicants searched PubMed database for articles that contained the term "peptide synthetase," Applicants found 181 articles containing the term. However, only 67 articles were published before Applicants' effective filing date (see Exhibit B). Furthermore, since it is obvious from examination of the titles of many of the patents and articles found that they do not pertain to methods of combinatorial synthesis,

Applicants do not believe that the search would create an undue burden on the Examiner. Therefore, Applicants request that the election of species in subgroups 1-5 and 7-13 be withdrawn.

Applicants respond to the substitute election of species as follows:

Subgroup 1: Species of Starter Unit

The Examiner states that, for the purposes of searching, Applicants must elect a single species of starter unit that shows all the atoms and bonds that are necessary to define the starter unit.

Applicants elect compound 2 shown in Figure 2.

Claims that read on the elected starter unit are Claims 1-3, 5-12, and 14-21.

Subgroup 2: Species of Handle

The Examiner states that, for the purposes of searching, Applicants must elect a single species of handle that shows all the atoms and bonds that are necessary to define the handle.

Applicants elect the handle shown in compound 2 of Figure 2 (enclosed in the box).

Claims that read on the elected handle include Claims 1-3 and 5-21.

Subgroup 3: Species of Solid Support Unit

The Examiner states that, for the purposes of searching, Applicants must elect a single species of solid support unit that shows all the atoms and bonds that are necessary to define the solid support and all the atoms and bonds that are necessary to define the handle.

Applicants have not specified any species of solid support unit throughout the specification and the claims but instead have referred to the solid support unit generically. However, Applicants have indicated that when an alkyne handle is used on the starter unit, the solid support should also be functionalized with an alkyne (see page 9, lines 16-20 of the specification).

Claims that read on the elected solid support are Claims 1-3 and 5-21.

Subgroup 4: Species of Template Structure

The Examiner states that, for the purposes of searching, Applicants must elect a single species of template structure that will result in a particularly defined core structure that is shared by all members of the library or is a representative example of the library.

One of the advantages of Applicants' claimed method is that it can generate a library having diverse template (or core) structures (see page 2, lines 25-31 of the specification). Since a library prepared by Applicants' claimed method typically will have a large diversity of core structures, Applicants have not indicated in the specification or claims any species of template that would be obtained using a peptide synthetase (the species of enzymatic machinery that Applicants have elected below). However, Applicants have indicated that an amino acid based pathway, such as peptide synthetases, would utilize functionalized derivatives of amino acids as starter units, such as the modified amino acid starter unit shown in shown in Figure 2, compound 2, that are feed to the enzymatic machinery (see page 7, lines 24-26 of the specification). Therefore, templates that are produced by the enzymatic machinery would incorporate amino acid derivatives within their structure.

Claims that read on template structures that could be derived from peptide synthetase are Claims 1-3, 5-12, and 14-21.

#### Subgroup 5: Species of Template Structure after Functionalization

The Examiner states that, for the purposes of searching, Applicants must elect a single species of template structure after functionalization that has a particularly defined core structure that is shared by all members of the library or has a core structure that is a representative example of the library.

As discussed above, a library prepared by Applicants' claimed method typically will have a large diversity of core structures. Therefore, Applicants have not indicated in the specification or claims any particular species of template after functionalization. However, Applicants have indicated that an amino acid based pathway, such as peptide synthetases, would utilize functionalized derivatives of amino acids as starter units, such as the modified amino acid starter unit shown in shown in Figure 2, compound 2, that are feed to the enzymatic machinery (see page 7, lines 24-26 of the specification). Therefore, templates that are produced by the enzymatic machinery would incorporate amino acid derivatives within their structure. The amino acid derivatives incorporated into the template would have latent functional groups, such as the functional groups present on amino acid side chains, which could be further functionalized (see page 13, lines 29-31 of the specification). For example, the tyrosine derivative starter unit shown in figure 2, compound 2 has a hydroxy group that could be functionalized by reaction with an

electrophile, such as an isocyanate, an anhydride, or an acid chloride (see page 14, lines 8-18 of the specification).

Claims that read on functionalized template structures that could be derived from peptide synthetase are Claims 1-3, 5-12, and 14-21.

#### Subgroup 6: Species of Enzymatic Machinery

The Examiner states that, for the purposes of searching, Applicants must elect a single species of enzymatic machinery.

Applicants elect peptide synthetase.

The claims that read on the elected enzymatic machinery are Claims 1-3, 5-12, and 14-21.

#### Subgroup 7: Species of Unnatural Natural Product

The Examiner states that, for the purposes of searching, Applicants must elect a single species of unnatural natural product that has a particularly defined core structure that is shared by all members of the library or has a core structure that is a representative example of the library.

A library prepared by Applicants' claimed method typically will have a large diversity of core structures which can be chemically modified or which can be prepared from a starter unit that has been chemically modified to form unnatural natural products. Therefore, Applicants have not indicated in the specification or claims any particular species of nonnatural natural product. However, as discussed above, Applicants have indicated that an amino acid based pathway, such as peptide synthetases, would utilize functionalized derivatives of amino acids as starter units, such as the modified amino acid starter unit shown in shown in Figure 2, compound 2, that are feed to the enzymatic machinery (see page 7, lines 24-26 of the specification). Therefore, templates that are produced by the enzymatic machinery would incorporate amino acid derivatives within their structure. The amino acid derivatives incorporated into the template would have latent functional groups, such as the functional groups present on amino acid side chains, which could be further functionalized (see page 13, lines 29-31 of the specification). For example, the tyrosine derivative starter unit shown in figure 2, compound 2 has a hydroxy group that could be functionalized by reaction with an electrophile, such as an isocyanate, an anhydride, or an acid chloride (see page 14, lines 8-18 of the specification).

Claims that read on unnatural natural products that could be derived from peptide synthetase are Claims 1-3, 5-12, and 14-21.

Subgroup 8: Species of Chemical Reaction

The Examiner states that, for the purposes of searching, Applicants must elect a single species of chemical reaction.

Applicants elect Mitsunobu reaction to generate alcohols from an amide. However, Applicants would like to point out that typically the a template structure would be functionalized with more than one reaction since one advantage of solid phase combinatorial chemistry is that multi-step reactions can be carried out without labor intensive purification steps (see page 12, lines 5-9 of the specification).

Claims that read on the elected chemical reaction are Claims 1-3 and 5-21.

Subgroup 9: Species of Genetically Modified Enzyme

The Examiner states that, for the purposes of searching, Applicants must elect whether or not the enzymatic machinery is genetically modified.

Applicants elect the species of enzymatic machinery that has no genetic modification.

Claims that read on the elected machinery (subgroup 6) that is not genetically modified are Claims 1-3, 5-11, and 14-21.

Subgroup 10: Species of Antibody Element (Claim 14)

The Examiner states that, for the purposes of searching, Applicants must elect whether or not the starter unit includes an antibody recognition element.

Applicants elect the species of starter unit that has no antibody recognition element.

The claims that read on the elected starter unit (subgroup 2) that does not have an antibody recognition element are Claims 1-3, 5-12, and 15-21.

Subgroup 10: Species of Antibody Element (Claim 15)

The Examiner states that, for the purposes of searching, Applicants must elect whether or not the template includes an antibody recognition element.

Applicants elect a template that has no antibody recognition element.

The claims that read on a template (subgroup 4) that does not have an antibody recognition element are Claims 1-3, 5-12, and 16-21.

Subgroup 11: Species of Combinatorial Technique

The Examiner states that, for the purposes of searching, Applicants must elect a single species of combinatorial technique.

Applicants elect parallel synthesis as a species of combinatorial technique.

Claims that read on Applicants' elected species of combinatorial technique are Claims 1-3, 5-21.

Subgroup 12: Species of Biomolecule

The Examiner states that, for the purposes of searching, Applicants must elect a single species of biomolecule.

Applicants elect polysaccharides as a species of biomolecule. However, Applicants would like the Examiner to note that more than one type of biomolecule may be attached to one template structure (see page 14, lines 28-30 of the specification).

Claims that read on the elected biomolecule are Claims 1-3, 5-21.

Subgroup 13: Species of Encoding Technique

The Examiner states that, for the purposes of searching, Applicants must elect a single species of encoding technique.

Applicants elect nuclear magnetic resonance spectroscopy as a species of encoding technique.

Claims that read on the elected species of encoding technique are Claims 19-21.

Applicant would like to thank Examiner Epperson for discussing the above species elections with Applicants attorney on May 5, 2003 and May 6, 2003. If a telephone conversation would further clarify any issues, or help expedite prosecution of this case, Applicants invite the Examiner to contact the undersigned at (617) 248-5150.

A Petition for Extension of Time under 37 CFR 1.136 and the appropriate fee are submitted herewith. Please charge any additional fees associated with this filing, or apply any credits, to our Deposit Account No. 03-1721.

Respectfully Submitted,



Theresa A. Devlin, Ph.D.

Reg. No.: 45,361

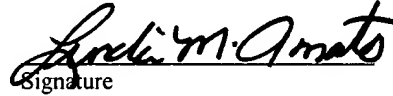
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Linda M. Amato

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